

### REMARKS

This paper is filed in response to the Office Action mailed February 8, 2008. Claims 3, 5, 32, 39, 40, 48, 50, 77, 84-85, and 95-125, 127-129 and 146 are withdrawn from consideration. Claims 1, 6, 9, 12-14, 16, 17, 33, 36, 45, 51, 54, 55, 61, 62, 78, 81, 126 and 130-145 are rejected. Claims 1, 45, 126, 130 and 140 have been amended herein. Claims 6, 51, 132, 138 and 139 have been canceled herein. Amendments have been made without prejudice or disclaimer. No new matter has been added. Reconsideration is respectfully requested.

### Election/Restrictions

Applicant acknowledges that claims 127-129 and 146 have been withdrawn as allegedly being directed to a non-elected invention.

### Specification

The specification is objected to as allegedly failing to provide proper antecedent basis for the term "a rate of  $10^{-6}$  or greater" as found in claims 6, 51, 126 and 132. However, applicants submit that the specification provides sufficient support and antecedent basis for the instant claims.

More particularly, applicant respectfully submits that paragraph [0577] of the published application discloses that a DNA polymerase for use in the present invention has a proofreading function which provides a mismatched base (mutation) in a base

sequence at a rate of  $10^{-6}$ ,  $10^{-3}$  and  $10^{-2}$ . The terms and phrases used in the claims have clear support or antecedent basis in the description as required by 37 C.F.R. 1,75(d)(1). Furthermore, as stated by MPEP § 608.01(o), an applicant is not limited to the nomenclature used in the application as filed, but should have clear support or antecedent basis in the specification. Applicant submits that it clear that a proofreading function with a mutation rate of  $10^{-3}$  and  $10^{-2}$  is greater than a mutation rate of  $10^{-6}$ . Therefore, the claim term "a rate of  $10^{-6}$  or greater" as found in claims 6, 51, 126 and 132, has clear support or antecedent basis in the specification as filed.

As such, applicants request the removal of the objection to the specification.

**Rejection—35 U.S.C. 102(b)**

Claims 130-140 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Morrison *et al.* (*EMBO J.*, 1993), as evidenced by Burgers (*Chromosoma*, 1998). Applicant respectfully traverses the rejection of the claims under 35 U.S.C. § 102(b) because Morrison *et al.* fail to teach each and every element of the remaining claims.

Morrison *et al.* disclose yeast strains comprising the *pol3-01* mutation introduced into the yeast chromosome by targeted integration using the YlpAM26 plasmid containing a mutated yeast *POL3* (Morrison *et al.*, page 1471, last paragraph; page 1472, second full paragraph).

Amended independent claim 130 recites modifying at least one amino acid position in a 3' to 5' exonuclease active site of at least one DNA polymerase operable in at least one eukaryotic cell in a manner that increases the error-prone frequency of DNA replication in the at least one eukaryotic cell such that the at least one DNA polymerase provides mismatched bases at a frequency of  $10^{-6}$  or greater, wherein the at least one DNA polymerase is a DNA polymerase expressed in the at least one eukaryotic cell with a plasmid expression vector. Morrison *et al.* does not disclose a DNA polymerase expressed in the at least one eukaryotic cell with a plasmid expression vector as required by amended independent claim 130.

Therefore, for at least the reasons discussed herein, amended independent claim 130, and those claims dependent therefrom, are patentable over Morrison *et al.* Accordingly, Applicant requests that the claim rejections under 35 U.S.C. § 102(b) in light of Morrison *et al.* be removed.

**Rejection—35 U.S.C. 103 (a)**

Claims 1, 6, 9, 12-14, 16, 17, 33, 36, 45, 51, 54, 55, 61, 62, 78, 81, 126, 141 and 142-144 are rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Morrison *et al.* (*EMBO J.*, 1993) and Burgers (*Chromosoma*, 1998), in view of Tanabe *et al.* (EP 1054057, 2000) and del Cardayre *et al.* (U.S. 6,379,964).

Amended independent claims 1, 45 and 126 recite, in part, modifying at least one amino acid position in a 3' to 5' exonuclease active site of at least one DNA polymerase

and, wherein the at least one DNA polymerase is expressed with a plasmid expression vector. Morrison *et al.* and Burgers, as discussed previously, do not recite the expression of a DNA polymerase with a plasmid vector. Likewise, Tanabe *et al.* and del Cardayre *et al.* do not disclose or discuss the expression of a DNA polymerase with a plasmid expression vector. Therefore, it would not have been obvious to one of skill in the art, in view of the cited references, to arrive at the present invention.

As such, applicant respectfully requests the removal of the rejection of claims 1, 6, 9, 12-14, 16, 17, 33, 36, 45, 51, 54, 55, 61, 62, 78, 81, 126, 141 and 142-144 under 35 U.S.C. 103(a).

**Rejection—35 U.S.C. 112**

*35 U.S.C. 112, first paragraph*

Claims 1, 6, 9, 12-14, 16, 17, 33, 36, 45, 51, 54, 55, 61, 62, 78, 81, 126 and 130-145 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter not enabled by the specification. Claim 1, 45, 126 and 130 have been amended to recite that the DNA polymerase provides mismatched bases at a frequency of  $10^{-6}$  or greater. Therefore, applicant respectfully submits that the claims pending in the Application are fully enabled by the specification. Therefore, in view of the foregoing remarks and the proposed claim amendments, Applicant respectfully requests removal of the claim rejections under 35 U.S.C. § 112, first paragraph.

### **Double Patenting**

Claims 1, 6, 9, 12-14, 16, 17, 33, 36, 45, 51, 54, 55, 61, 62, 78, 81, 126 and 130-145 are provisionally rejected under nonstatutory obviousness-type double patenting as allegedly being unpatentable over claims 1, 2, 4, 6-47, 49, 51-76, 78-83, and 86-89 of co-pending Application No. 10/550,924.

Applicant continues to note the double patenting rejection and respectfully reserves response until the notice of allowable subject matter.

CONCLUSION

In view of the foregoing, it is believed that all of the claims are patentable in their present form, and a prompt notice of allowance for this case is respectfully requested. As mentioned above, if the Examiner finds any remaining impediment to the prompt allowance of this application, please contact the undersigned attorney.

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Respectfully submitted,

/Yury M. Colton/

Yury M. Colton  
Attorney for Applicant  
Registration No. 55,081

STOEL RIVES LLP  
201 South Main Street  
Salt Lake City, Utah 84111  
Telephone: (801) 578-6998  
Facsimile: (801) 578-6998